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Abstract: Temporality enters our immediate experience as passage and becoming: the role time plays in the construction of a world of enduring entities tends to go unnoticed. This paper examines the relation between time and ontology in the context of unilateral neglect, a neuropsychological syndrome in which patients fail to perceive or respond to stimuli in the contralateral hemifield, behaving as if that half of space does not exist. Traditional models characterize neglect exclusively in spatial terms. Based on recent investigations suggesting abnormal temporal dynamics, here we highlight the impact of time factors on the presentation of the disorder. Neglect patients do not simply miss the presence of stimuli on the left: they also ignore the past as well as the future of neglected stimuli. We claim that, if this occurs, it is because time, and not only space, is impaired.

Torino, 05/05/2006

Dear Editor,

We modified the manuscript in an attempt to achieve the top standard required for publication in *Neuropsychologia*.

Reviewer 1

The reviewers have answered most of my concerns to my satisfaction. However, there is still a one-sentence paragraph on page 3, and the formatting appears to need revision on page 17.

We would like to thank the reviewer for her/his careful review of our manuscript. We have now integrated the one-sentence paragraph on page 3. Formatting on page 17 has been revised.

On page 10, there is a typing mistake: the word "that" should be replaced by "than" in the second to last paragraph.

We apologize for the typing mistake. As requested we have now replaced “that”.

Best regards,

Cristina Becchio

Cesare Bertone

Time and neglect: abnormal temporal dynamics in unilateral spatial neglect

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Abstract. Temporality enters our immediate experience as passage and becoming: the role time plays in the construction of a world of enduring entities tends to go unnoticed. This paper examines the relation between time and ontology in the context of unilateral neglect, a neuropsychological syndrome in which patients fail to perceive or respond to stimuli in the contralateral hemifield, behaving as if that half of space does not exist. Traditional models characterize neglect exclusively in spatial terms. Based on recent investigations suggesting abnormal temporal dynamics, here we highlight the impact of time factors on the presentation of the disorder. Neglect patients do not simply miss the *presence* of stimuli on the left: they also ignore the past as well as the future of neglected stimuli. We claim that, if this occurs, it is because time, and not only space, is impaired.

Keywords: unilateral neglect, time, temporal abnormalities, loss of awareness.

Depending on the severity of the pathology, neglect may be noticed merely by observing patients' spontaneous behaviour: patients with neglect may not notice objects on the left of a scene, may not eat food on the left side of the plate, may ignore the left part of words. When asked to write, they may only use the right side of the page. Similarly, if asked to copy or draw an object they may neglect to report elements on the left, drawing in fact only half of it.

These bewildering behavioural manifestations clearly exhibit a *spatial* gradient: the patient behaves as if half of the space does not exist, failing to report, react or search for stimuli located in the space contralateral to the lesion. The spatial nature of neglect is manifest and, understandably, interest in research has focused on spatial mechanisms (Halligan, Fink, Marshall, & Vallar, 2003). Here, we intend to focus on a dimension that, although less evident, is nevertheless no less important in the presentation of the disorder: *time*.

Compared with spatial cognition, little is known about the neuropsychology of time. In this paper we first summarize the results of recent investigations suggesting abnormal temporal dynamics in neglect. Next, we consider some of the empirical and theoretical issues raised by this evidence: do the temporal abnormalities observed in neglect reflect the impairment of a unique mechanism or do they arise in relation to different timing systems? Do temporal deficits in neglect relate to spatial distortions? A final concern relates to the contribution of temporal deficits to neglect *per se*, i.e. to the loss of awareness for contralateral stimuli and events characteristically observed in neglect patients. It is impossible for us – wrote Kant in the *Critique of Pure Reason* (1787) – to represent things outside space and time and this is because things appear to us as spatio-temporally connoted. Whereas previous work focused on the role of spatial encoding, here we highlight time factors. Neglect patients do not simply miss the *presence* of stimuli on the left: they also ignore the *past* as well as the *future* of neglected stimuli. We claim that, if this occurs, it is because time, and not only space, is impaired.

Temporal abnormalities at different temporal scales

Temporal abnormalities in neglect are revealed in temporal integration (Duhamel, Goldberg, Fitzgibbon, Sirigu, & Grafman, 1992; Heide, Blankenburg, Zimmermann, & Kömpf, 1995), as well as in temporal processing (Husain, Shapiro, Martin, & Kennard, 1997; Hillstrom, Husain, Shapiro, & Rorden, 2004) and in retaining information over time (Husain, Mannan, Hodgson, Wojciulik, Driver, & Kennard, 2001; Pisella, Berberovic, & Mattingley, 2004). One source of ambiguity is that these abnormalities are measured over a wide range of timescales, from milliseconds to seconds and minutes. Here we consider three different intervals or timescales: temporal abnormalities at the scale of tens to hundred milliseconds, abnormalities in the range of 400 ms, and finally, abnormalities in the range of seconds.

100¹ ms: maintaining stable representations of visual stimuli across saccades

Despite our impression of a full and coherent world as immediate and instantaneous, ‘seeing’ is itself a temporal fact, requiring an integration over time (Humphreys, 1997). Since visual information is sampled at high resolution over only a few degrees of visual angle at the fovea, a complete representation of a scene requires the contents of individual eye fixations to be integrated over space and time (Resink, 2000). During monitoring of a visual scene, we move our eyes constantly, performing large saccades during inspection of the global scene, and smaller saccades when sampling information at a smaller spatial scale. In the primary visual cortex, the retinal image is constructed anew at each eye fixation, overwriting all previously encoded information. Without re-mapping to maintain and re-locate neural activity corresponding to these inputs, this general overwriting phenomenon would extend further, leading to the disappearance of relevant information across ocular shifts: the world would appear as a sequence of non-integrated visual snapshots, at different spatial scale (Pisella & Mattingley, 2004).

¹ 100 ms is the duration of a saccade covering a 40° angular displacement.

Re-mapping deficits in neglect are suggested by studies requiring the use of a double-step paradigm (Duhamel et al., 1992; Heide et al. 1995).

Insert Figure 1 about here

In this paradigm, two sequentially flashed targets (A and B) must be fixated by two consecutive saccades departing from a central fixation point toward A, and then from A to B. When the two targets are extinguished within 180 ms – too short a period of time to direct eye movements to both targets prior to them being removed from the display - the generation of a spatially accurate second saccade requires a re-mapping. This process allows the oculo-motor system to anticipate the new position of B by integrating the displacement on the retina produced by the first saccade toward position A with oculo-motor information.

This process of re-mapping has been shown to be disrupted in one patient showing neglect in consequence of frontoparietal damage (Duhamel et al., 1992). The patient performed well with targets flashed first into the right field and then into the left field. When she was asked to do the same task with a target flashed first in the left field and then in the right field, she completed the first saccade correctly, but never acquired the second target, even though this required her to make a saccade in the ipsilesional direction.

Examining patients with unilateral lesions of various structures, Heide et al. (1995) found that both right and left lesions of the parietal posterior cortex (PPC) caused errors in double-step saccades. Each pair of targets was located either in the same hemifield (within-hemifield condition) or in different hemifields (between-hemifields condition). Both patients with right and left PPC lesions showed an elevated percentage of errors when in double-step saccades that involved

crossing the midline (between-hemifields condition). In addition, patients with right PCC – all of whom initially showed neglect – showed significant errors under conditions in which double-step saccades had to be performed entirely within the left visual field.

Several lines of evidence support the proposal that the poster parietal cortex may have an important role in keeping track of spatial locations over saccades (see Leon and Shadlen, 2003). A basic model of spatial re-mapping deficits in neglect was recently proposed by Pisella and Mattingley (2004). The model accounts for the differential pattern of errors between right and left lesions (Heide et al., 1995), postulating a hemispheric asymmetry for re-mapping. According to this model, with damage to the left parietal posterior cortex, any saccade, directed toward the left or right visual field, results in a re-mapping deficit affecting the representation of the visual field located on the side opposite the direction of the saccade (i.e. the previous left visual field after a rightward saccade, the previous right visual field after a leftward saccade). With damage to the right posterior parietal cortex (patients with left neglect), leftward and rightward orienting produces different consequences: whereas after rightward saccade, only the previous left visual field is overwritten, leftward orienting results in a general loss of awareness for the locations of objects in both hemifields

400 ms: abnormal temporal dynamics of visual attention

Individuals without any neurological abnormality experience a significant loss of attention after engaging a target for the purpose of identification (Raymond, Shapiro, & Arnell, 1992; Shapiro, Arnell, & Raymond, 1997; Duncan, Humphreys, & Ward, 1997). This loss of temporal attention, known as ‘attentional blink’, is usually attributed to an inability to retain usable representation of a second target while completing attentive processing of a first target.

A standard procedure for quantifying this loss of temporal attention requires individuals to view a rapid serial visual presentation (RSVP) of letters presented successively at the same location. All the letters in the sequence are black except one, which is white. This is the first target the

subject is asked to identify. In half trials, this first target is followed, at some point in the sequence, by a black “X” (second target). Healthy observers require about 400 ms between targets to be able to report both targets accurately. Using this standard procedure, Husain et al. (1997) found that neglect patients have an abnormally severe and protracted attentional blink, lasting nearly three times as long as for healthy observers.

Husain *et al.* (1997) examined the attentional blink at one central location. In a recent single-case study Hillstrom et al. (2004) varied the location of the second target: whereas the first target was always presented at fixation, the second target appeared either at fixation or peripherally to the left or right. This variation led to an interesting finding: the patient with left-side neglect showed a prolonged attentional blink in identifying the second stimulus when the second stimulus appeared contralesionally, an attentional blink of normal duration when the stimulus appeared at fixation and no significant attentional blink when the second stimulus appeared ipsilesionally. These results suggest that the temporal dynamics of attentional processing may be enhanced compared to normal performance for ipsilesional stimuli, whereas it is significantly prolonged for stimuli appearing to the left. This suggestion of an atypically good performance on the right is consistent with previous investigations, which demonstrated ‘hyperattention’ toward stimuli on the right at the expense of stimuli to the left (De Renzi, Gentilini, Faglioni, & Barbieri, 1989; Di Pellegrino, Basso & Frassinetti, 1997; Gainotti, D’Erme, & Bartolomeo, 1991; Ladavas, Petronio, & Umiltà, 1990; Smania, Martini, Gambina, Tomelleri, Palamara, Natale, & Marzi, 1998).

On the side of temporal perception, a spatio-temporal gradient in the allocation of attention may explain the distortion observed in evaluating temporal intervals. For example, Basso, Nichelli, Frassinetti, & Di Pellegrino (1996) examined time perception at different spatial locations in a patient showing severe left-sided neglect. The patient tended to overestimate the stimuli on the left side and, conversely, to underestimate those on the right side. This distortion was observed both in an interval comparison (300/700 ms) task and with a time production (1 s) paradigm.

Other studies focused on the issue of simultaneity and temporal order. Using a temporal order paradigm, Rorden, Mattingley, Karnath, & Driver (1997) found that patients may not be aware of objective simultaneity. In this study, patients were presented with two visual events, occurring on either side of fixation at various temporal asynchronies. The task was to judge which of two events (left or right) occurred first while maintaining fixation. Typically, healthy participants judge the temporal order of the events correctly at asynchronies greater than 40 ms. In contrast, when required to say which stimulus is presented first, neglect patients consistently reported the ipsilesional item as appearing first unless the contralesional item had a substantial lead (200 ms or more). This effect, known as “prior entry”, is found both in the visual modality and the auditory modality (Karnath, Zimmer, & Lewald, 2002).

Recently Baylis, Simon, Baylis, & Rorden (2002) tested how extinction is affected by the introduction of a temporal asynchrony at the onset of two visual stimuli presented in the two hemifields. In a first experiment patients were asked to identify the stimuli. All patients showed maximal extinction when the stimuli were physically simultaneous. In a second experiment, the same patients were requested to report which stimulus was presented first. All patients required the contralesional item to have a significant lead in order to be judged as occurring first.

1 to 15 sec : impaired spatial working memory

When neglect patients perform cancellation tasks it is frequently observed that they search over territory on the ipsilesional side that they have searched before. This amnesic aspect of exploration – called ‘re-visiting behaviour’ – was for example described by Wojciulik, Husain, Clarke, & Driver (2001) in a left neglect patient with right inferior frontal and basal ganglia damage. As in the cancellation tasks commonly used in clinical assessment, the patient was required to cancel visual targets (Os) in a display of scattered items (other letters). In one condition, the patient used a pen that left a visible mark; in a second condition, the same pen was used with its cap on, so that no visible marks were left and the patient needed to remember the location of items already cancelled.

Despite the instruction to cancel each target only once, the patient re-cancelled several targets in the invisible mark condition, suggesting that his working memory could not retain the locations of visited items. These re-cancellations were eliminated by substituting Os with drawings of common objects of different shapes, each object having a unique identity. Consistently with the hypothesis of a specifically *spatial* working memory impairment, these results suggest that non-spatial memory was intact and could prevent re-cancellations.

Husain et al. (2001) confirmed this conclusion in a neglect patient with parietal damage, by measuring eye movements during visual search. The patient was also asked to click on a response button only when fixating a target that was judged to be a new discovery, not when re-fixating an old target that had previously been found and clicked. The study found that target locations on the right side were frequently re-fixated and, more importantly, were also treated as new discoveries at an abnormally high rate. Interestingly, the frequency of such revisiting was correlated with the performance in standard clinical tests measuring the severity of neglect.

Mannan, Mort, Hodgson, Driver, Kennard, & Husain (2005) recently extended the study to 16 neglect patients with lateralized damage. MRI mapping of lesions allowed the authors to distinguish between two types of pathological 're-clicking' associated with different areas of damage. Neglect patients with right inferior frontal lesion demonstrated a constant or even decreasing probability of re-clicking over time, presumably depending on failure to inhibit responses to rightward locations. In contrast, for neglect patients with damage to the right intraparietal sulcus, the probability of re-clicking on a target increased with time (and saccades) from the initial discovery. Because they rarely re-clicked at short intervals, this pattern of behaviour suggests a deficit in keeping track of locations during extended search.

Although these results may be consistent with an impairment in spatial working memory, several alternative interpretations warrant further consideration. First, because the time and number of intervening saccades are not independently manipulated, increased re-clicking cannot be attributed to a deficit in memory that is independent of saccadic eye movement. Furthermore, in

cancellation tasks, remembering the locations of items is incidental to the primary task of visual search. A natural question might thus be whether the same impairment would arise when no re-mapping is required and patients are explicitly instructed to remember the location of objects in a visual array.

This issue was addressed by Pisella, Berberovic and Mattingley (2004) using a change-detection task in which participants were instructed to remember either the spatial locations, colours or shapes of a small number of items. They found that parietal patients were significantly worse in detecting changes in the location of visual objects relative to changes in their colour or shape. Crucially, this selective impairment in detecting changes in location only occurred when a 1 s delay was introduced between stimulus presentation and response.

A direct measure of the spatial working memory capacity in neglect was recently provided by Malhotra, Jäger, Parton, Greenwood, Playford, Brown, Driver, & Husain (2005) using a variant of the traditional Corsi task. To disambiguate working memory processes from lateral biases leading to competition between target locations at encoding, all stimuli were arranged vertically in a columnar array. After a sequence of spatial locations had been displayed, a single location was probed visually, with subjects indicating verbally if it had been presented in the preceding sequence. Despite stimuli being presented vertically, neglect patients performed significantly worse than stroke patients without neglect.

In the study by Malhotra et al. (2005), stimuli were displayed on the vertical meridian of the screen. Ferber and Danckert (2006) found the same difficulty in maintaining spatial locations for stimuli displayed vertically and on the right side only. Again, neglect patients performed significantly worse than neurologically intact participants and right-brain damaged controls.

How many “times” are impaired in neglect?

The exploration of spatial deficits in neglect has provided evidence of neurobiological distinction between different frames of reference and regions of space: egocentric versus allocentric frame of

reference, far versus near space, personal versus extrapersonal space, perceptual versus motor impairment (Halligan et al., 2003). In this respect, the neuropsychological syndrome of unilateral spatial neglect has become a strong and increasingly relevant tool to dissect the functional and anatomical architecture of the systems involved in spatial cognition.

A natural question arising with respect to the temporal abnormalities observed in neglect patients is thus: Do these abnormalities reflect the impairment of a unique temporal mechanism? Do they arise in relation to different timing systems?

Although observing an impairment at different timing scales may provide a relevant clue, future studies are needed to establish whether dissociated neural levels are involved. As for spatial cognition, we might thus discover that temporal cognition also involves a complex set of independent, although related, systems (for a review of the current timing literature, see, for example, Mauk and Buonomano, 2004).

A further question, arising from the consideration of the preceding one, is how temporal deficits relate to the lateralized spatial bias in neglect. Are spatial and temporal deficits independent of each other, or are they linked? Very few studies have addressed this issue. As the following analysis shows, the answer appears to be highly dependent on the timescale considered.

A spatial gradient in temporal dynamics is suggested for temporal processing at the timescale of 400 milliseconds. In a pioneering study, di Pellegrino, Basso and Frassinetti (1998) investigated the time for selection in a neurological patient with left-sided extinction. Using a variant of the attentional blink paradigm, they found a longer selection time for stimuli presented in contralesional space than in ipsilesional space. Similarly, Hillstrom et al. (2004), demonstrated an interacting temporal and spatial gradient of difficulty in shifting attention from one stimulus to another in a patient with neglect: when the second target appeared on the left, the patient required more time between targets to identify both accurately, compared to when the second target appeared at fixation or to the right.

These results suggest a spatial, *horizontal* gradient in the allocation of attention. Recently, Snyder and Chatterjee (2004) addressed the question of whether a spatial gradient may modulate temporal processing for stimuli presented on a *vertical* axis. This hypothesis was tested on a patient with an acute temporal-parietal stroke, showing extinction for contralesional visual stimuli. The experiment found that for vertically aligned stimuli the patient was poorer at judging the order of events in contralesional space than in ipsilesional space. More important, his performance improved with stimuli with larger vertical separations, as if limitations in awareness of successive events close in time could be compensated by greater distance in space.

Is a similar spatial gradient shown by temporal deficits at the level of seconds?

Recent studies suggest a negative answer. Pisella, Berberovic, & Mattingley (2004) found that the impairment in detecting location changes over brief delays (1s) is equivalent across all horizontal positions in space. Consistent with the view that a spatial working memory impairment in neglect is not restricted to contralesional locations, Malhotra et al. (2005) demonstrated a deficit in maintaining spatial locations on purely vertical tasks. Ferber and Danckert (2006) found the same difficulty in maintaining spatial locations for stimuli displayed vertically, on the putatively non-neglected side of space.

Contrary to working memory deficits, re-mapping deficits exhibit a spatial gradient. With respect to temporal abnormalities at higher scales, the difference is in the coordinate system. At the timescale of re-mapping (10-100 ms) the spatial gradient is expressed with respect to the direction of the gaze shift, rather than to the horizontal position. The model by Pisella and Mattingley (2004) postulates an asymmetry between leftward and rightward orienting: whereas after rightward saccade, only the previous left visual field is overwritten, leftward orienting results in a general loss of awareness for the locations of objects in both hemifields. The re-mapping deficits are thus spatialized, however with respect to the direction of gaze.

Insert Table 1 about here

Taken together these findings suggest that interaction between the spatial and temporal gradient of impairment depends on the scale of representation: whether temporal abnormalities reflect a spatial gradient depends on the timescale considered. A further aspect to be taken into account is the frame of reference in relation to which to measure the spatial gradient. Categorizing temporal abnormalities into different timescales allows us refine the notion of a spatio-temporal interaction, suggesting that different spatial frames may be involved at different timescales.

The above mentioned evidence concerns perceptive processes. A recent study by Bartolomeo, Bachoud-Lévi, Azouvi, & Chokron (2005) suggests that interactive spatio-temporal dynamics may also affect imagination. In the study, right-brain damaged patients were invited to conjure up a visual mental image of the map of France. They subsequently had to state whether auditorily presented towns or regions were situated to the left or right of Paris on the imagined map. Compared to non-neglect patients, neglect patients were slower for left than for right imagined location. This chronometric exploration of representational neglect suggests that under certain circumstances prolonged dynamics of attention may affect not only visual neglect, but also mental imagery abilities.

What is the contribution of temporal abnormalities to neglect?

Research on neglect has primarily been concerned with what patients with neglect can do *despite* their apparent lack of awareness. The lack of awareness per se, its nature, the paradoxes it raises, have attracted comparatively little interest (Halligan and Marshall, 1998).

In the first part of this paper we presented temporal abnormalities from research carried out at the functional level of neuropsychological systems. In the following, we address the issue of the contribution of temporal abnormalities to the phenomenology of neglect, i.e. to the loss of

awareness for contralateral stimuli and events. How is it possible for an individual to lose half of the world, maintaining an apparently intact representation of the other half? Does a breakdown of spatial representation constitute a sufficient explanation?

The idea that neglect patients may suffer from a 'representational map reduced to one half' was presented to the scientific community with the Piazza del Duomo experiment, being Piazza del Duomo a well-known square in Milan (Bisiach and Luzzati, 1978). The authors asked two patients with right-brain lesions to imagine themselves at one end of the square and describe all the business places around the square. As one would expect in the hypothesis of a defect of space representation, both patients failed to recall shops, cafes, etc., on the left.

The next step in the experiment was for subjects to imagine themselves looking at the cathedral from the opposite end of the square. Remarkably, in this latter condition, patients named the previously neglected places but omitted those recalled just a few moments before.

In discussing the theoretical implication of these results, Bisiach and Luzzati (1978) focused on the spatial domain, i.e. on the possibility that neglect may occur at the level of the internal representation of space, without concomitant visual input from the environment. This observation unambiguously suggested the representational nature of the disorder, or at least of some manifestations of it. The failure - proposed the authors - was to be explained as damage to the contralateral portion of the internal representation of space.

The problem with this explanation is that it seems to account for the first part of the experiment, but not for its continuation. Having imagined the square from one given vantage point, patients were in fact required to imagine it from the opposite perspective.

This shift of perspective shows that patients did indeed recall both halves of the square, the only trouble is that they did not recall them at the same time. The problem admits various formulations:

1. Since the two halves that the patients report make a whole piazza, why cannot the whole piazza be reported? (Halligan and Marshall, 1998). Why didn't they stick the two halves together?
2. Describing first one half of the square, then the other half, patients provide in fact two inconsistent descriptions of the same object. Given that a few minutes elapsed between the first report and the second and that neglect preserves reasoning abilities, how is it possible for them not to be aware of the contradiction?
3. Finally, if they remember all the places around the square, why don't they acknowledge that something in their description is missing?

Beyond space: a dissociation in time

The experimental paradigm of Bisiach and Luzzati (1978) was used by many subsequent studies. Employing this same paradigm, Rode, Rossetti, Perenin, & Boisson (2004) found, for example, that geographic information has to be spatialized to be neglected. In this study, a patient with persistent representational neglect was tested for his abilities to mentally evoke the map of France in two different conditions: in the first condition, he had to list all the towns he could "see" on the imagined map, in the second condition, he simply had to remember the names of as many French towns as possible. Left representational neglect was observed in the first condition only, when an iconic representation was required, whereas no deficit was observed when geographic information had to be accessed through a purely semantic mode. This result suggests a dissociation between a dual mode of coding and retrieval information from memory: visuo-spatial versus semantic.

Ortigue, Viaud-Delmon, Annoni, Landis, Michel, Blanke, Vuilleumier, & Mayer (2001) report an analogous dissociation between co-ordinate systems in a right-brain damaged patient asked to mentally visualize the Place Neuve in Geneva. The patient systematically omitted items on his left side when the mental representation had to be generated with respect to his own body

position. Nonetheless, he succeeded perfectly when he only had to use allocentric spatial relationships between the different items.

Such reports of dissociated performance may be interpreted as dissociations between different modes of coding (visuo-spatial versus semantic) or different co-ordinate systems (egocentric versus allocentric). What renders the Piazza del Duomo experiment so puzzling is that here the dissociation intervenes between two halves, homogeneous in space as well as in the mode of coding. What is it then that prevents the patient from sticking them together?

Berti and Rizzolatti (1992) propose that the encoding of space is a necessary prerequisite for conscious perception. If spatial encoding is prevented or impaired, as it is in neglect, the presence of the stimulus does not enter consciousness. With respect to the Piazza del Duomo experiment, a lack of spatial awareness *per se* does not however seem to constitute a sufficient explanation: a spatially constrained disorder of awareness (Berti, 2000) might explain why, at any one moment, the patient is unable to represent the whole scene, not why the two halves do not form a whole.

If this occurs, it must be because the two halves of the square do not co-exist at the same time.

Time and ontology: permanence, simultaneousness, succession

Objects in the real world frequently move in and out of view, as when they pass behind occluding surfaces. Such occlusion disrupts the spatio-temporal continuity of items on the visual field. Yet occlusion does not disrupt the continuing existence of the objects in the scene (Michotte 1950).

Imagine observing an object, for example a car, emerging from behind a building. The apparition of the object in the perceptive field marks the beginning of the presence of the object, but not the beginning of its existence: the object appears as pre-existent.

Imagine observing the same object as it passes by and disappears behind another building. The object ceases to be visible, but continues to exist after its disappearance. The surface of the building prevents the object from being perceived, yet the object still exists, so that the observer expects to

see it reappear. Despite the interruption in spatio-temporal continuity, the object continues to exist, pre-existing the moment of its apparition (*permanence of anteriority*), and persisting *in time* after its disappearance (*permanence of posteriority*; Becchio & Bertone, 2003).

Both these forms of permanence appear to be in some way disrupted in neglect. Differently from occlusion, neglect not only suspends the perceptive presence of objects, but it also interrupts their existence. As noted by J. J. Gibson, there are two quite different ways in which an object may disappear and appear. It may *go out of sight* or *come into sight*, on the one hand, and it may *go out of existence* or *come into existence* on the other (Gibson, Kaplan, Reynolds, & Wheeler, 1969).

Neglect seems to entail this latter form of disappearance. The elements that from time to time fall in the left hemi-space do not simply go out of sight: disappearing from the patient's representation, they also disappear from his conception. This implies that the patient affected by neglect does not simply ignore the *presence* of spatial elements on the left: the permanence these elements in the past as well as their persistence in the future must be impaired. This would explain why in the Piazza del Duomo experiment the patient fails to acknowledge any contradiction or manifest the awareness that something is missing. The left half of space neither pre-exists nor persists in the patient's representation, which, in fact, behaves as if this half of space – and the elements that from time to time fall in it – *has never existed* and *will never exist*. A change of viewpoint, as requested in the experiment, thus has an ontological effect: one side of the space ceases to exist, the other side explodes into existence. The result is a sequence of hemi-structures independent both in time and ontology.

“Things” wrote Kant in the *Analytic of Principles* (*Critic of Pure Reason*, 1787) “are coexistent, in so far as they exist in one and the same time. But how can we know that they exist in one and the same time? Only by observing that the order in the synthesis of apprehension of the manifold is arbitrary and a matter of indifference, that is to say, that it can proceed from A, through B, C, D, to E, or contrariwise from E to A.” This possibility is interrupted in neglect, preventing the

patient from proceeding from one half of the space to the other half. In this way, the two halves of the square emerge as structures completely independent in time.

Insert Figure 2 about here

As Kant inferred, “...let us assume that in a number of substances considered as phenomena each is completely isolated, that is, that no one acts upon another... the coexistence of these cannot be an object of possible perception and that the existence of one cannot, by any mode of empirical synthesis, lead us to the existence of another”.

In normal conditions, temporal processing allows the integration of successive perception in a world of temporally enduring entities. Items successively selected co-exist within a continuous space-time. Disrupting the temporal continuity between one side of the space and the other, neglect not only prevents the representation of half the space, but renders impossible a temporal continuity between successively represented hemi-spaces.

Of course, this breakdown in spatio-temporal continuity does not exclude that the information relative to the neglected hemi-space might be retrieved, for example, through a semantic mode of access (e.g. Rode et al., 2004). By claiming that in neglect half of space ceases to exist we do not intend to suggest that the information relative to the left side of space is definitely lost. As Berti (2000) noted, in neglect it is not the representation and the awareness of the stimuli *per se* that are impaired, but their representation in the left space. What the present analysis adds to this interpretation is the role of the temporal component. A spatial constrained disorder may explain the loss of half of space in present, but does not account for the ontological effects entailed by neglect. Elsewhere we described the consequences of neglect as an ontological slide (see Becchio & Bertone, 2005). Extending the disappearance to the past and future of objects, an impairment of the temporal dimension may represent one critical impairment resulting in this slide.

Conclusive considerations

If we consider the phenomena of neglect, what is striking is not so much simply that the patient fails to represent half the space, but rather that he does not conceive it.

We claimed that a spatial deficit may explain why the patient does not represent, at any given time, half of the space, but it does not in fact account for the patient's inability to conceive it.

This inability suggests that the representation of the left side of space is not only defective in the present, but that it is not maintained over time.

Recent investigations support this interpretation, showing that combined with a lateralized spatial bias to the right, neglect may imply temporal abnormalities at various scales. Such abnormalities, we surmise, play a crucial role in explaining why half of the world gets lost in neglect, i.e. why the patient with neglect behaves as if that half of space does not exist (*in the present*), has never existed (*in the past*) and will never exist (*in the future*)

When we think of time, we think of how events follow on from one another, we rarely consider that time enters in the constitution of a world of enduring entities (Becchio and Bertone, 2003). Neglect implies an impairment of temporal mechanisms, thus dramatically disclosing the link between time and ontology.

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References

- Bartolomeo, P., Bachoud-Lévi, A-C., Azouvi, P., & Chokron, S. (2005). Time to imagine space: a chronometric exploration of representational neglect. *Neuropsychologia*, *43*, 1249-1257.
- Basso, G., Nichelli, P. Frassinetti, F., & Di Pellegrino, G. (1996). Time perception in a neglected space. *Cognitive Neuroscience and Neuropsychology*, *13*, 2111-2114.
- Baylis, G.C., Simon, S.L., Baylis, L.L., & Rorden, C. (2002). Visual extinction with double simultaneous stimulation: what is simultaneous? *Neuropsychologia*, *40*, 1027-1034.
- Becchio, C., & Bertone, C. (2003). Object temporal connotation. *Brain and Cognition*, *52*, 192-196.
- Becchio C., & Bertone, C. (2005). The ontology of neglect. *Consciousness and Cognition*, *14*, 483-494.
- Berti, A. (2000). Neuropsychological syndromes and the structure of conscious processes. In *The Emergence of the Mind. Proceedings of the 9th International Symposium*. Milan, Fondazione Carlo Erba.
- Berti, A., & Rizzolatti, G. (1992). Visual processing without awareness: evidence from unilateral neglect. *Journal of Cognitive Neuroscience*, *4*, 345-351.
- Bisiach, E., & Luzzati, C. (1978). Unilateral neglect of representational space. *Cortex*, *14*, 129-133.
- De Renzi, E., Gentilini, M., Faglioni, P., & Barbieri, C. (1989). Attentional shift towards rightmost stimuli in patients with left visual neglect. *Cortex*, *25*, 231-237.
- Di Pellegrino G., Basso G., & Frassinetti F. (1997). Spatial Extinction on double asynchronous stimulation. *Neuropsychologia*, *35*, 1215-1223
- Di Pellegrino G., Basso G., & Frassinetti F. (1998). Visual extinction as a spatio-temporal disorder of selective attention. *NeuroReport*, *9*, 835-839.

- Duhamel, J.R., Goldberg, M.E., Fitzgibbon, E.J., Sirigu, A., & Grafman, J. (1992). Saccadic dysmetria in a patient with right frontoparietal lesion. *Brain*, *115*, 1387-1402.
- Duncan, J., Humphreys, J., & Ward, R. (1997). Competitive brain activity in visual attention. *Current Opinion in Neurobiology*, *7*, 255-261.
- Ferber, S., & Danckert, J.(2006). Lost in space – The fate of memory representations for non-neglected stimuli. *Neuropsychologia*, *44*, 320-325.
- Gainotti, G., D’Erme, P., & Bartolomeo, P. (1991). Early orientation of attention toward the half space ipsilateral to the lesion in patients with unilateral brain damage. *Journal of Neurology, Neurosurgery and Psychiatry*, *54*, 1082-1089.
- Halligan, P.W., Fink, G.R., Marshall, J.C., & Vallar, G. (2003). Spatial cognition: evidence from visual neglect. *Trends in Cognitive Sciences*, *3*, 125-133.
- Halligan, P.W., & Marshall, J.C. (1998). Neglect of awareness. *Consciousness and Cognition*, *7*, 356-380.
- Heide, W., Blankenburg, M., Zimmermann, E., & Kömpf, D. (1995). Cortical control of double-step saccades: implications for spatial orientation. *Annals of Neurology*, *38*, 739-748.
- Heide, W., & Kömpf, D. (1997). Specific parietal lobe contribution to spatial constancy across saccades. In P. Thier & H. Karnath (Eds.), *Parietal lobe contribution to orientation in 3D space* (pp.515-526). Heidelberg: Springer.
- Hillstrom, A., Husain, M., Shapiro, K., & Rorden, C. (2004). Spatiotemporal dynamics of attention in visual neglect: a case study. *Cortex*, *40*, 433-440.
- Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., & Kennard, C. (2001). Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brain*, *124*, 941-952.

- Husain, M., Shapiro, K., Martin, J., & Kennard, C. (1997). Abnormal temporal dynamics of visual attention in spatial neglect patients. *Nature*, *385*, 154-156.
- Humphreys, G.W. (1997). A vision over time and space. *Nature*, *385*, 120-121.
- Kant, I. (1787). *Kritic der Reinen Vernunft*. Trans. Critique of Pure Reason, Norman Kemp Smith. New York: St. Martin's Press, 1929.
- Karnath, H.O., Zimmer, U., & Lewald, J. (2002). Impaired perception of temporal order in auditory extinction. *Neuropsychologia*, *40*, 1977-1982.
- Ladavas, E., Petronio, A., & Umiltà, C. (1990). The deployment of visual attention in the intact field of hemineglect patients. *Cortex*, *26*, 307 – 317.
- Leon, M.I., & Shadlen, M.N. (2003). Representation of time by neurons in the posterior parietal cortex of the macaque. *Neuron*, *38*, 317-327.
- Malhotra, P., Jäger, H., Parton, A., Greenwood, R., Playford, E., Brown, M., Driver, J., & Husain, M. (2005). Spatial working memory capacity in unilateral neglect. *Brain*, *128*, 424-435.
- Mannan, S., Mort, D., Hodgson, T., Driver, J., Kennard, C., & Husain, M. (2005). Revisiting previously searched locations in visual neglect: role of right parietal and frontal lesions in misjudging old locations as new. *Journal of Cognitive Neuroscience*, *17*, 340-354.
- Mauk, M.D., & Buonomano, D.V. (2004). The Neural Basis of Temporal Processing. *Annual Review Neuroscience*, *27*, 304-340.
- Ortigue, S., Viaud-Delmon, I., Annoni, J.M., Landis, T., Michel, C., Blanke, O., Vuilleumier, P., & Mayer, E. (2001). Pure representational neglect after right thalamic lesion. *Annals of Neurology*, *50*, 401-404.

- Pisella, L., Berberovic, N., & Mattingley, J.B. (2004). Impaired working memory for location but not for colour or shape in visual neglect: a comparison of parietal and non-parietal lesions. *Cortex*, *40*, 379-390.
- Pisella, L., & Mattingley, J.B. (2004). The contribution of spatial remapping impairments to unilateral visual neglect. *Neuroscience and Biobehavioral Reviews*, *28*, 181-200.
- Raymond, J.E., Shapiro, K.L., & Arnell, K.M. (1992). Temporary suppression of visual processing in an RSVP task: an attentional blink? *Journal of Experimental Psychology. Human perception and performance*, *18*, 849-860.
- Resink, R.A. (2000). The dynamic representation of scenes. *Visual cognition*, *7*, 17-42.
- Rode, G., Rossetti, Y., Perenin, M., & Boisson, D. (2004). Geographic information has to be spatialised to be neglected: a representational neglect case. *Cortex*, *40*, 391-397.
- Rorden, C., Mattingley, J.B., Karnath, H.O., & Driver, J. (1997). Visual extinction and prior entry: impaired perception of temporal order with intact motion perception after unilateral parietal damage. *Neuropsychologia*, *35*, 421-433.
- Shapiro, K.L., Arnell, K.M., & Raymond, J.E. (1997). The attentional blink: a view on attention and a glimpse on consciousness. *Trends in Cognitive Sciences*, *1*, 291-296.
- Smania, N., Martini, M.C., Gambina, G., Tomelleri, A., Palamara, A., Natale, E., & Marzi, C.A. (1998). The spatial distribution of visual attention in hemineglect and extinction patients. *Brain*, *121*, 1759-1770.
- Snyder, J.J., & Chatterjee, A. (2004). Spatial-temporal anisometries following right parietal damage. *Neuropsychologia*, *42*, 1703-1708.
- Wojciulik, E., Husain, M., Clarke, K., & Driver, J. (2001). Spatial working memory deficit in unilateral neglect. *Neuropsychologia*, *39*, 390-396.

Figure 1. Example of a double-step stimulus with the two targets A, and B, being flashed successively while the gaze is directed to a central fixation point (FP). When both saccades are performed after all targets have disappeared, the generation of a spatially accurate second saccade (from A to B) requires anticipating the outcome of the first saccade and programming the second saccade based on the anticipated end-point of the first (A). If subjects based their saccades on retinal position alone, their second saccades would end on B' instead of B. Redrawn from Heide & Kömpf (1997).

Figure 2. In normal conditions, the features of the square, independently from the order in which they have been mentioned, form a unitary spatio-temporal structure, in which they simultaneously exist. In neglect, the features that from time to time fall within the ipsilesional space are bound together in an independent structure. The simultaneousness is preserved within each aggregate, but not between the features of different aggregates. (t: time)

Table 1. Relation between spatial and temporal abnormalities in neglect.

	Does the temporal deficit relate to a spatial bias?	
10 – 100 ms	✓	Asymmetry between leftward and rightward orienting
400 ms	✓	Interacting temporal and spatial gradient of difficulty in shifting attention from one stimuli to another
1-15 s		Spatial working memory deficit equivalent across all horizontal positions in space

Figure 1

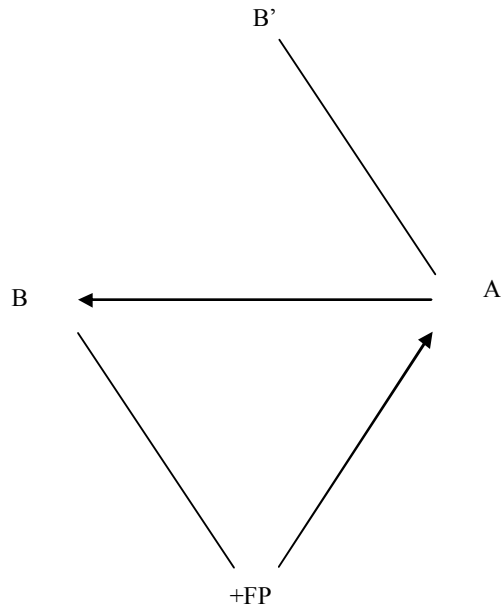


Figure 2

